

Claims

1. Nucleic acid which codes for the  $\alpha$  chain of a human T cell receptor, or for a functional derivative or a fragment thereof and which comprises a CDR3 region formed from a combination of a V $\alpha$ 20 and J $\alpha$ 22 gene segment.

2. Nucleic acid which codes for the  $\alpha$  chain of a human T cell receptor, or for a functional derivative or a fragment thereof and comprises a CDR3 region selected from:

(a) a nucleotide sequence coding for the amino acid sequence (SEQ ID NO: 23)

Y C L (X<sub>1</sub>...X<sub>n</sub>) S A R Q L T F (I)

in which X<sub>1</sub> ... X<sub>n</sub> represents a sequence of 3-5 amino acids,

(b) a nucleotide sequence which codes for an amino acid sequence which is at least 80 % identical with the amino acid sequence from (a), or

(c) a nucleotide sequence which codes for an amino acid sequence with an equivalent recognition specificity for the peptide component of the T cell receptor ligands.

Wnt desc

I  
3. Nucleic acid as claimed in claim 2,  
w h e r e i n  
the amino acid sequence  $X_1 \dots X_n$  is selected from  
the group comprising the amino acid sequences VGG,  
VLSG, ATG, VSG, DSG, VVSG, ALAG, APSG and VGR.

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SUB  
F2  
7  
4. Nucleic acid as claimed in claim 3,  
w h e r e i n  
the amino acid sequence  $X_1 \dots X_n$  is selected from  
the group comprising amino acid sequences VGG, VLSG  
and ATG.

5. Vector,  
w h e r e i n  
it contains at least one copy of a nucleic acid as  
claimed in one of the claims 1 to 4.

6. Cell,  
w h e r e i n  
it expresses a nucleic acid as claimed in one of  
the claims 1 to 4.

7. Cell,  
w h e r e i n  
it is transformed with a nucleic acid as claimed in  
one of the claims 1 to 4 or with a vector as  
claimed in claim 5.

II  
8. Polypeptide,  
w h e r e i n  
it is coded by a nucleic acid as claimed in one of  
the claims 1 to 4.

II 9. Polypeptide as claimed in claim 8,  
w h e r e i n  
it comprises the variable domain of the  $\alpha$  chain of  
a human T cell receptor.

III 10. Nucleic acid which codes for the  $\beta$  chain of a human  
T cell receptor, or for a functional derivative or  
a fragment thereof and comprises a CDR3 region  
formed from a combination of a  $V\beta 22$  gene segment, a  
 $D\beta 1$  or  $D\beta 2$  gene segment and a  $J\beta$  gene segment in  
particular a  $J\beta 2.1$ ,  $J\beta 2.3$  or  $J\beta 2.7$  gene segment.

11. Nucleic acid which codes for the  $\beta$  chain of a human  
T cell receptor, or for a functional derivative or  
a fragment thereof and comprises a CDR3 region  
which is selected from:

2  
9  
C  
1  
(a) a nucleotide sequence coding for the amino acid  
sequence (SEQ ID NO: 24) and (SEQ ID NO: 45)  
respectively,

C A (X'<sub>1</sub> ... X'<sub>n</sub>) Y/D E Q Y F (II)

in which X'<sub>1</sub> ... X'<sub>n</sub> represents a sequence of  
5-7 amino acids,

(b) a nucleotide sequence coding for the amino acid  
sequence (SEQ ID NO: 25)

C A (X''<sub>1</sub> ... X''<sub>n</sub>) N E Q F F (III)

in which X''<sub>1</sub> ... X''<sub>n</sub> represents a sequence of  
5-7 amino acids,

- (c) a nucleotide sequence coding for the amino acid sequence <sup>(SEQ ID NO. 26)</sup>

C A (X''''<sub>1</sub> ... X''''<sub>n</sub>) D T Q Y F (IV)

in which X''''<sub>1</sub> ... X''''<sub>n</sub> represents a sequence of 5-7 amino acids,

- (d) a nucleotide sequence which codes for an amino acid sequence that is at least 80 % identical with an amino acid sequence from (a), (b) or/and (c), or
- (e) a nucleotide sequence which codes for an amino acid sequence with an equivalent recognition specificity for the peptide component of the T cell receptor ligand.

12. Nucleic acid as claimed in claim 11,

wherein

the amino acid sequence X'<sub>1</sub> ... X'<sub>n</sub> is selected from the group comprising <sup>(SEQ ID NO. 27)</sup> SSETNS, <sup>(SEQ ID NO. 28)</sup> SSETSS, <sup>(SEQ ID NO. 29)</sup> TSGTAS, <sup>(SEQ ID NO. 30)</sup> RSGTGS, <sup>(SEQ ID NO. 31)</sup> SSGTDS, <sup>(SEQ ID NO. 32)</sup> SSGTRS, <sup>(SEQ ID NO. 33)</sup> SSGSDS, <sup>(SEQ ID NO. 34)</sup> SSSTGS, <sup>(SEQ ID NO. 35)</sup> SSSTVS, <sup>(SEQ ID NO. 36)</sup> SSSTLS, <sup>(SEQ ID NO. 37)</sup> SSSTLF, <sup>(SEQ ID NO. 38)</sup> SSSTAS, <sup>(SEQ ID NO. 39)</sup> SSHTDS, <sup>(SEQ ID NO. 40)</sup> SSDTLS, and <sup>(SEQ ID NO. 41)</sup> SRWDSE.

13. Nucleic acid as claimed in claim 12,

wherein

the amino acid sequence X'<sub>1</sub> ... X'<sub>n</sub> represents <sup>(SEQ ID NO. 27)</sup> SSETNS, <sup>(SEQ ID NO. 31)</sup> SSGTDS, <sup>(SEQ ID NO. 29)</sup> TSGTAS, or <sup>(SEQ ID NO. 30)</sup> RSGTGS.

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14. Nucleic acid as claimed in claim 11,  
w h e r e i n  
the amino acid sequence X''<sub>1</sub> ... X''<sub>n</sub> represents  
(SEQ ID NO. 42) (SEQ ID NO. 43)  
SSGTSSY or SSDQGM or the amino acid sequence  
(SEQ ID NO. 44)  
X'''<sub>1</sub> ... X'''<sub>n</sub> represents SADSFK
15. Vector,  
w h e r e i n  
it contains at least one copy of a nucleic acid as  
claimed in one of the claims 10 to 14.
16. Cell,  
w h e r e i n  
it expresses a nucleic acid as claimed in one of  
the claims 10 to 14.
17. Cell,  
w h e r e i n  
it is transformed with a nucleic acid as claimed in  
one of the claims 10 to 14 or with a vector as  
claimed in claim 15.
18. Polypeptide,  
w h e r e i n  
it codes for a nucleic acid as claimed in one of  
the claims 10 to 14.
19. Polypeptide as claimed in claim 18,  
w h e r e i n  
it comprises the variable domain of the  $\beta$  chain of  
a human T cell receptor.
- II

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20. Polypeptide,  
wherein  
it has T cell receptor properties and is composed  
of a polypeptide as claimed in claim 8 or 9 as well  
as a polypeptide as claimed in claim 18 or 19 as  
subunits.
21. Polypeptide as claimed in one of the claims 8, 9,  
18, 19 or 20,  
wherein  
it is coupled to a labelling group or a toxin.
22. Polypeptide as claimed in one of the claims 8, 9,  
18, 19, 20 or 21,  
wherein  
it is present in an oligomerized form.
23. Antibody against a polypeptide as claimed in one of  
the claims 8, 9, 18, 19, 20, 21 or 22 which is  
directed against a region which is responsible for  
recognizing the peptide ligand.
24. Antibody as claimed in claim 23,  
wherein  
it is directed towards a CDR3 region.
25. T cell,  
wherein  
it contains a T cell receptor as claimed in claim  
20.



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VII

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26. Pharmaceutical composition which contains as active component a nucleic acid as claimed in one of the claims 1 to 4 or 10 to 14, a polypeptide as claimed in one of the claims 8, 9 or 18 to 23, a peptide ligand against the polypeptide, an antibody as claimed in claim 23 or 24 or a cell as claimed in claim 6, 7, 16, 17 or 25 optionally together with other active components as well as common pharmaceutical auxiliary agents, additives or carrier substances.
27. Use of a pharmaceutical composition as claimed in claim 26 for the production of an agent for the diagnosis of tumour diseases or a predisposition for a tumour disease.
28. Use of a pharmaceutical composition as claimed in claim 26 for the production of an agent for monitoring the course of the disease in a tumour disease.
29. Use as claimed in claim 27 or 28, *improver MDC*  
wherein the detection of T cells that express a polypeptide as claimed in claim 20 as the T cell receptor is carried out in a sample liquid by a nucleic acid hybridization assay, an immunoassay, a test for the binding of specific peptide ligands or a specific T cell activity test.
30. Use of a pharmaceutical composition as claimed in claim 26 for the production of an agent for the prevention or therapy of a tumour disease.



unproven MDC

31. Use as claimed in claim 30, wherein the agent is suitable for the stimulation of the growth of T cells that express a polypeptide as claimed in claim 20 as a T cell receptor.
32. Use as claimed in claim 31, wherein the agent is suitable for growth stimulation of the T cells in vivo.
33. Use as claimed in claim 31 or 32, wherein the agent for growth stimulation comprises the peptide ligand of the T cell receptor or/and the entire molecule from which the peptide ligand is derived or a fragment thereof.
34. Use as claimed in claim 31 or 32, wherein the growth stimulation includes an antibody that specifically activates the T cell receptor.
35. Use as claimed in claim 31, wherein the growth stimulation is carried out by isolating specific T cells, in vitro expansion and subsequent administration of expanded T cells.
36. Use as claimed in one of the claims 27 to 35, wherein the tumour disease is a kidney cell carcinoma.



37. Process for the isolation of T cells that express a polypeptide as claimed in claim 20 as a T cell receptor,  
w h e r e i n  
a sample containing T cells is contacted with an agent that binds specifically to the CDR3 region of the T cell receptor, T cells that react with the agent are identified and optionally separated from other T cells.
38. Process as claimed in claim 37,  
w h e r e i n  
the agent is selected from the peptide ligand of T cells, a MHC peptide complex containing the peptide ligand or/and an anti-TCR antibody.
39. Process as claimed in claim 37 or 38 additionally comprising an in vitro expansion of T cells.
40. Process for the isolation of T cells which express a polypeptide as claimed in claim 20 as the T cell receptor,  
w h e r e i n  
nucleic acid sequences that code for the T cell receptor are introduced into a T cell line and are made to express therein.
41. Process for the isolation of T cells that express a polypeptide as claimed in claim 20 as the T cell receptor,  
w h e r e i n  
nucleic acid sequences which code for the T cell

are introduced into t  
and the T cells are iso  
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sses a polypeptide as c  
cell receptor.  
  
or the identification o  
receptor as claimed in  
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tain a cDNA bank,  
  
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nsfection with HLA-A\*0  
r (ii) HLA-A\*0201 posi  
are used,  
  
ng the transfected rec  
ability to stimulate  
  
ifying a cDNA sequence  
ntigen which contains t

42. Transgenic animal,  
w h e r e i n  
it expresses a polypeptide as claimed in claim 20  
as the T cell receptor.
43. Method for the identification of peptide ligands of  
a T cell receptor as claimed in claim 20 comprising  
the steps:
- (a) isolating RNA from tumour tissue,
  - (b) converting the RNA into double-stranded cDNA  
molecules,
  - (c) introducing the cDNA molecules into host cells  
to obtain a cDNA bank,
  - (d) transfecting eukaryotic recipient cells with  
aliquots of the cDNA bank wherein (i)  
cotransfection with HLA-A\*0201 DNA is carried  
out or (ii) HLA-A\*0201 positive recipient  
cells are used,
  - (e) testing the transfected recipient cells for  
their ability to stimulate T cells,
  - (f) identifying a cDNA sequence which codes for  
the antigen which contains the peptide ligand  
and

(g) identifying the sequence of the peptide ligand.

44. Method as claimed in claim 43,  
w h e r e i n  
step (e) comprises testing for the ability to lyse  
TNF-sensitive cells.

ad 4

all GI

$$\frac{d}{dt} \left( \frac{\partial L}{\partial \dot{x}} \right) = \frac{\partial L}{\partial x}$$